



NOTES

INFERTILITY & FETAL LOSS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Disorders that adversely affect the function of the female reproductive system fertility

SIGNS & SYMPTOMS

- See individual disorders

DIAGNOSIS

DIAGNOSTIC IMAGING

- Ultrasound

LAB RESULTS

- Serum hormonal levels

OTHER DIAGNOSTICS

- Obstetric history

TREATMENT

- See individual disorders

AMENORRHOEA

osms.it/amenorrhoea

PATHOLOGY & CAUSES

- Abnormal menstruation cessation/absence in biologically female people of reproductive age, not related to menopause/pregnancy/lactation

TYPES

- Primary amenorrhoea
 - Failure to reach menarche by age 15 years
- Secondary amenorrhoea
 - Previously regular menses ceases for three months or longer

RISK FACTORS

- Hypothalamic-pituitary-gonadal axis does not induce cyclic changes in the endometrium
 - Hypothalamic dysfunction (e.g. **GnRH deficiency**, traumatic injury, functional (stress, excessive exercise, **eating disorders**, systemic illness)
 - Pituitary dysfunction (e.g. empty sella syndrome, **pituitary tumor**/infarct)
 - Ovarian dysfunction (e.g. primary ovarian insufficiency (POI), **Turner syndrome**, **FMR1** mutation)
- Psychogenic amenorrhea
 - Pseudocyesis (false pregnancy)

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- Outflow tract disorders
 - E.g. **Müllerian agenesis** (Mayer–Rokitansky–Kuster–Hauser syndrome), intrauterine adhesions (Asherman syndrome)
- Other
 - **Polycystic ovary syndrome** (PCOS)
 - Hypo/**hyper**thyroidism
 - Hormone receptor abnormalities
 - Enzyme deficiencies

COMPLICATIONS

- Infertility
- Osteoporosis
- Psychological distress

SIGNS & SYMPTOMS

- Menses absent
- Clinical presentation of causative disorder

DIAGNOSIS

- Evaluate secondary sexual characteristics (Tanner staging)
- Discrepancy in Tanner stage and age may indicate constitutional puberty delay, Turner syndrome
- ↑ body mass index (BMI) + hyperandrogenism signs (acne, hirsutism) may indicate PCOS

DIAGNOSTIC IMAGING

Pelvic ultrasound/hysteroscopy

- Detects structural abnormalities

Head MRI

- Identifies pituitary anomalies

LAB RESULTS

- ↑ hGH indicates pregnancy
- ↑ serum prolactin indicates pituitary adenoma, prolactinoma
- Follicle stimulating hormone (FSH)
 - ↑ level indicates Turner syndrome, primary ovarian insufficiency (POI)

- ↓ level indicates functional hypothalamic amenorrhea/hypothalamic-pituitary disorders

- ↓ luteinizing hormone level indicates functional hypothalamic amenorrhea/hypothalamic-pituitary disorders
- ↓ estradiol indicates abnormal ovarian function
- ↑ free and total testosterone indicates PCOS, ovarian/adrenal tumor

OTHER DIAGNOSTICS

- Progesterone challenge test
 - Oral medroxyprogesterone administered daily for 7–10 days → withdrawal bleeding when hormone stopped indicates adequate endogenous estrogen level, rules out outflow tract abnormality
 - If no withdrawal bleeding, administer estrogen + progestin daily for 10 days → failure to bleed indicates abnormal endometrium
- Karyotype
 - E.g. Turner syndrome (45,X), Müllerian agenesis (46,XX)
- Genetic testing
 - Fragile X syndrome (FMR1) associated with primary ovarian insufficiency

TREATMENT

MEDICATIONS

- Hypothalamic dysfunction
 - Oral contraceptives if pregnancy not desired, gonadotropins if pregnancy desired
- Ovarian insufficiency
 - Estrogen, progesterone replacement

SURGERY

- **Tumor:** surgical resection
- Surgically correct anatomic abnormalities preventing outflow

PSYCHOTHERAPY

- If functional hypothalamic dysfunction, address underlying cause (e.g. eating disorder)

OTHER INTERVENTIONS

- Specific treatments for causative morbidities (e.g. PCOS, thyroid disorders)
- Treat complications (e.g. estrogen replacement therapy, calcium + vitamin D supplements)

HORMONE CHANGES IN PRIMARY AMENORRHOEA

SIGN	GnRH	FSH	ESTROGEN & PROGESTERONE
GROWTH DELAY (CONSTITUTIONAL)	↓	↓	At pre-puberty levels
HYPOGONADOTROPIC HYPOGONADISM	↓	↓ or normal	↓
HYPERGONADOTROPIC HYPOGONADISM	↑	↑	↓
ANOVULATION	↑ or ↓	Normal	↑ Estrogen ↓ Progesterone
ANATOMIC ABNORMALITY	Normal	Normal	Normal

ECTOPIC PREGNANCY

osms.it/ectopic-pregnancy

PATHOLOGY & CAUSES

TYPES

- Ectopic pregnancy
 - Pregnancy in which fertilized ovum is implanted at site other than uterine endometrium
- Heterotopic pregnancy (rare)
 - Concurrent ectopic pregnancy and intrauterine pregnancy

CAUSES

- Altered anatomy/function (e.g. impaired tubal motility)

- Inflammatory-induced tubal damage, distorted/blocked patency → disrupted blastocyst progress to endometrial implantation site
- Ectopic sites
 - Fallopian tube (most common site, especially ampullary region)
 - Cervical
 - Abdominal
 - Ovarian
 - Interstitial/cornual (implantation where fallopian tube passes through myometrium)
 - Uterine cesarean scar

RISK FACTORS

- Previous tubal pregnancy
- Cesarean section history
- Endometriosis
- Infection, pelvic inflammatory disease (e.g. **salpingitis**)
 - **Chlamydia**: damages cilia lining fallopian tube
 - **Gonorrhea**: causes clubbed fimbriae, blocked/tortuous tube
- Previous pelvic surgery
- Congenital anomalies
- Tumors
- **Smoking** (dose-dependant)
- Vaginal douching
- **Risk increases with age**
- Intrauterine device (IUD) use (past and present)
- Use of assisted reproductive technologies (ART)
- In utero diethylstilbestrol (DES) exposure

COMPLICATIONS

- Rupture of fallopian tube or other structures, leading to profound bleeding
 - May be life-threatening
- Pregnancy loss
- Infertility
- A significant cause of pregnancy-related maternal mortality in first trimester

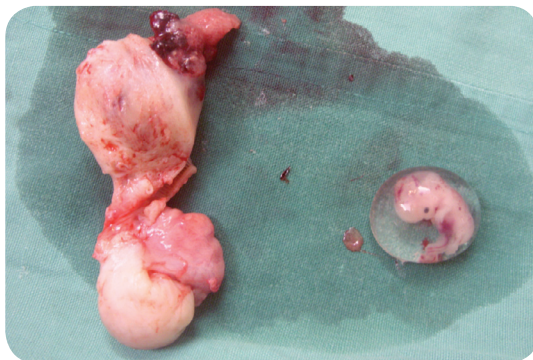


Figure 126.1 A ruptured cornual ectopic pregnancy following surgical removal. The fallopian tube (left) is distended at the junction with the cornu. The fetus is present on the right with an intact embryonic sac.

SIGNS & SYMPTOMS

- May be asymptomatic before rupture
- Common triad of symptoms
 - Variable bleeding (spotting/intermittent/hemorrhage)
 - **Lower abdominal pain/tenderness** (abrupt/slow, continuous/intermittent)
 - **Menses absent**
- Other symptoms
 - Normal early pregnancy discomforts (e.g. nausea, breast tenderness)
- Symptoms of rupture (surgical emergency)
 - Severe abdominal pain (may refer to shoulder with phrenic nerve irritation; rebound tenderness, guarding indicates peritoneal irritation)
 - Hemodynamic instability (feeling faint, syncope; tachycardia; hypotension; diaphoresis)

DIAGNOSIS

- Pelvic examination
 - Can identify source of bleeding
- Gentle adnexal palpation (light pressure to avoid rupture)
 - Palpable mass, cervical motion, adnexal, abdominal tenderness

DIAGNOSTIC IMAGING

Ultrasound

- Combination of empty uterus on ultrasound with a positive pregnancy test can confirm diagnosis
- If hemodynamically unstable
 - **Abdominal Focused Assessment with Sonography for Trauma (FAST)**: detects peritoneal bleeding, indicates rupture
- If stable
 - **Transvaginal ultrasound (TVUS)**: locates anatomical pregnancy site

LAB RESULTS

- ↑ serum human chorionic gonadotropin indicates pregnancy

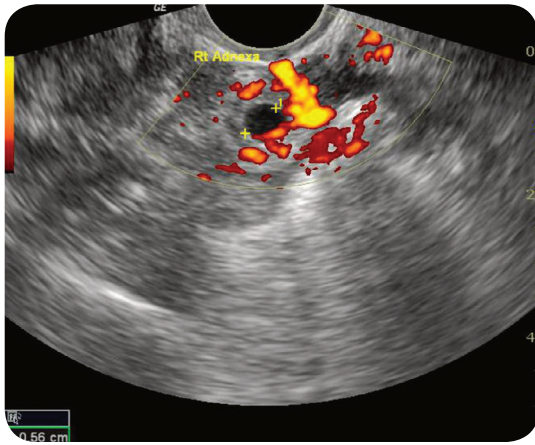


Figure 126.2 A Doppler ultrasound scan of the pelvis demonstrating the ring of fire sign in an individual with a tubal ectopic pregnancy.

TREATMENT

MEDICATIONS

- If unruptured
 - **Methotrexate**: folic acid antagonist inhibits DNA synthesis, cellular replication

SURGERY

- If ruptured, laparoscopic surgery
 - **Salpingectomy**: fallopian tube removal (standard practice)
 - **Salpingostomy**: tubal incision to remove tubal gestation only

OTHER INTERVENTIONS

- Stabilization measures if hemodynamic compromise is evident

MISCARRIAGE

osms.it/miscarriage

PATHOLOGY & CAUSES

- Loss of pregnancy < 20 gestation weeks
 - AKA spontaneous abortion

TYPES

- Complete
 - Spontaneous passage of all products of conception
- Incomplete (inevitable)
 - Bleeding, partially dilated cervix, ruptured membranes, products of conception remain in utero
- Threatened
 - Embryo/fetus jeopardized by bleeding, viable pregnancy, closed cervix
- Missed
 - Intrauterine fetal death that is not expelled
- Recurrent
 - History of $\geq$ three spontaneous pregnancy losses

RISK FACTORS

- Prior miscarriage
- Multiparity
- Advanced maternal age
- Smoking, substance abuse (e.g. cocaine)
- **Chromosomal abnormalities** (e.g. aneuploidies)
- **Structural uterine anomalies** (e.g. cervical insufficiency, **fibroids**)
- Maternal infections
 - Bacterial vaginosis
 - Toxoplasmosis
 - Coxsackie virus infection
 - Paramyxovirus infection (measles, mumps)
- Maternal comorbidities
 - **Thrombophilia**: $\uparrow$ decidual thrombosis risk
 - **Hypothyroidism**: thyroid peroxidase autoantibodies $\rightarrow$ may impair thyroid function during pregnancy
 - **Diabetes mellitus**: poor glycemic control

TYPES OF MISCARRIAGES

TYPE OF MISCARRIAGE	CHARACTERISTICS	PELVIC EXAM	ULTRASOUND EXAM
COMPLETE	Bleeding and complete passage of products of conception	Cervix: open or closed depending on stage of abortion	Empty uterus
INCOMPLETE	Heavy bleeding which includes passage of some products of conception	Cervix: dilated	Retained tissues
THREATENED	Slight vaginal bleeding Abdominal pain may be present Intact membranes	Cervix: closed	Viable intrauterine pregnancy detected
MISSED	Often asymptomatic	Cervix: closed	Nonviable pregnancy; retained products with no fetal cardiac activity or empty gestational sac
RECURRENT	History of ≥ 3 spontaneous abortions (may be missed, inevitable, incomplete, complete)	Depends on type	Empty uterus; uterine anomalies may be evident
INEVITABLE	Vaginal bleeding and abdominal pain present Membranes may/may not be ruptured	Cervix: dilated	Pregnancy may be viable or nonviable at time of presentation

(teratogenic effects of hyperglycemia; maternal vascular disease → uteroplacental insufficiency)

- **Systemic lupus erythematosus:** uteroplacental insufficiency, antiphospholipid antibodies, lupus anticoagulant
- **Obesity:** may be related to insulin resistance
- Trauma
 - **Iatrogenic:** invasive intrauterine procedures (e.g. chorionic villus sampling, amniocentesis)
 - Other injuries
- Idiopathic

COMPLICATIONS

- Vaginal blood/clots/fetal tissue passage
- Infection (e.g. septic abortion related to infection and retained products of conception)
- Disseminated intravascular coagulation (DIC)
 - Missed abortion → retained products release chemical mediators → coagulopathy

SIGNS & SYMPTOMS

- Vaginal bleeding
- Cramping abdominal/suprapubic pain

DIAGNOSIS

- Internal digital examination
 - Evaluates cervical dilation
- Vaginal speculum exam
 - Determines cervical dilation, characteristics of blood or tissue

DIAGNOSTIC IMAGING

Ultrasound

- TVUS
 - < nine gestation weeks
- Transabdominal
 - ≥ nine gestation weeks

LAB RESULTS

- Urine
 - ↑ hCG confirms pregnancy
- Complete blood count
 - Evaluates blood loss degree
- Blood type and Rh(D) testing
 - Determines risk for isoimmunization

TREATMENT

MEDICATIONS

- Inevitable/incomplete/missed abortion (nonviable pregnancy)
 - *If medically stable*: medical evacuation (prostaglandin E1 analog, antiprogesterone); expectant management (allow for natural passage)
- Prophylaxis with Rh₀(D) immunoglobulin as indicated

SURGERY

- Inevitable/incomplete/missed abortion (nonviable pregnancy)
 - *If medically unstable*: surgical evacuation (dilation and curettage/ vacuum extraction)

OTHER INTERVENTIONS

- Complete abortion
 - No medical intervention
- Recurrent abortion
 - Screening for possible causes
- Threatened abortion (viable pregnancy)
 - Expectant management

MOLAR PREGNANCY

osms.it/molar-pregnancy

PATHOLOGY & CAUSES

- Benign **abnormal trophoblastic growth**, included in disease group called gestational trophoblastic disease (GTD)
 - AKA hydatidiform mole (HM)
- Premalignant disease with **potential to develop into gestational trophoblastic neoplasia** (GTN), which includes invasive mole, choriocarcinoma, placental site trophoblastic tumor, epithelioid

trophoblastic tumor

TYPES

- Classifications based on histopathology, karyotype

Complete hydatidiform mole

- Single sperm fertilizes enucleated egg → paternal DNA duplication
- Usually diploid **46,XX/46,XY**
- Contains paternal genetic material only

- No fetal cells present
- Potential to become invasive → malignant gestational trophoblastic disease (GTD)

Partial hydatidiform mole

- One (normal) egg fertilized by two sperm
- Usually triploid 69,XXX/69,XXY/69XYY
- Contains maternal and extra paternal genetic material
- Some fetal cells evident (e.g. amnion, RBCs)
- Not usually associated with choriocarcinoma (< 5%)

CAUSES

- When nonviable fertilized ovum implants in uterus → paternal gene overexpression → trophoblastic proliferation, vesicular placental villi swelling → nonviable pregnancy

RISK FACTORS

- Obstetric history
 - Previous molar pregnancy
 - Spontaneous abortion
 - Infertility
- Maternal age extremes (≤ 15 and > 35 years old)
- Low dietary carotene (vitamin A precursor) and animal fat is associated with partial mole

COMPLICATIONS

- Potential for malignancy and metastasis (pulmonary, CNS)
- Trophoblastic pulmonary emboli
- Complete mole (if diagnosed in second trimester)
 - $\uparrow \uparrow$ hCG levels → theca lutein cysts (multiloculated cysts due to ovarian hyperstimulation), hyperthyroidism, preeclampsia
 - Anemia may also be present

SIGNS & SYMPTOMS

- Missed menses
- Enlarging uterus, feeling of pelvic pressure
 - Partial mole: small or normal for gestational age

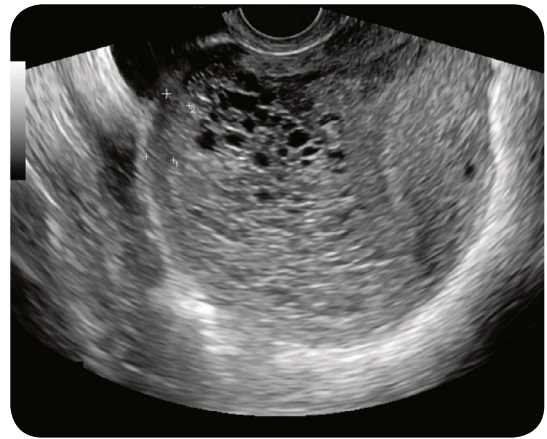


Figure 126.3 A transvaginal ultrasound scan demonstrating a mass within the uterus. The “bunch of grapes” sign is characteristic of a complete molar pregnancy.

- Complete mole: large for gestational age
- Hyperemesis gravidarum
 - Associated with $\uparrow \uparrow$ hCG
- First trimester uterine bleeding
 - Evident when molar villi separate from underlying decidua
 - Complete mole: dark, “prune juice”-colored discharge (accumulated, oxidized blood)
- Spontaneous passage of “grape-like” molar vesicles (hydropic villi)
- Hyperthyroidism
 - Tachycardia, warm skin, tremor, heat intolerance
- Preeclampsia
 - $\uparrow$ blood pressure

DIAGNOSIS

- Bimanual examination
 - Assess uterine size

DIAGNOSTIC IMAGING

Transvaginal ultrasound

- Complete mole
 - No embryo, fetus, or gestational sac visualized; absent fetal heartbeat
 - Absence of amniotic fluid
 - Numerous anechoic spaces contained

in a central heterogeneous mass:
snowstorm, **bunch of grapes**, or swiss
 cheese pattern

- Theca lutein cysts
- Incomplete mole
 - A fetus may be identified
 - Amniotic fluid is present
 - Chorionic villi echogenicity
 - Usually no theca lutein cysts

Chest X-ray

- Screen for metastasis

LAB RESULTS

- ↑↑ serum hCG
- Blood type and Rh(D) testing
 - Determines risk for isoimmunization
- Histopathologic analysis of evacuated material (definitive diagnosis)
 - Hydropic swelling of chorionic villi (cluster of grapes tissue)

OTHER DIAGNOSTICS

- Monitoring hCG levels to assess malignant transformation

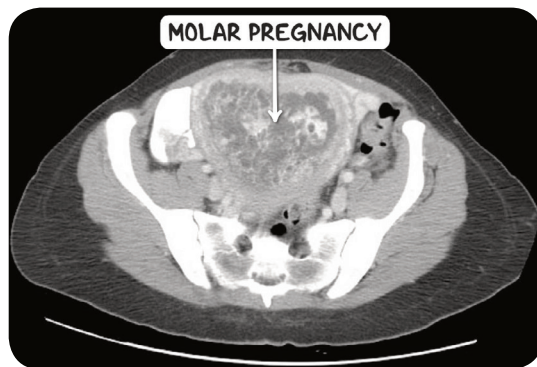


Figure 126.5 A CT scan of the pelvis in the axial plane demonstrating a molar pregnancy. The uterine corpus is distended by heterogeneously enhancing mass. There is no evidence of a fetus.

TREATMENT

- Uterine evacuation: suction and **curettage**

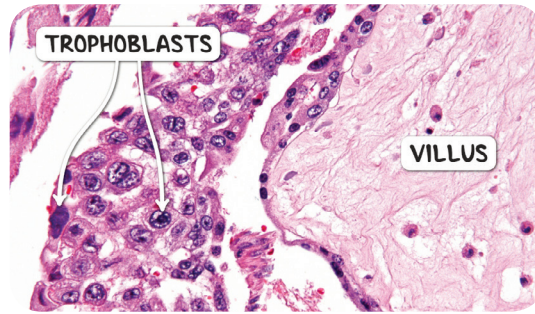


Figure 126.4 The histological appearance of a complete mole. The chorionic villi are expanded by loose fibrillar material (hydropic) and the overlying trophoblasts demonstrate marked atypical hyperplasia.

MEDICATIONS

- Actinomycin D
 - Chemoprophylaxis for complete mole
- Rh(D) immune globulin if indicated

SURGERY

- Hysterectomy
 - If ≥ 40 years old and/or do not wish further pregnancies

OTHER INTERVENTIONS

- Periodic (usually weekly) **monitoring of hCG levels** at regular intervals + reliable contraception until hCG is undetectable
 - Persistent elevation indicates postmolar gestational trophoblastic neoplasia

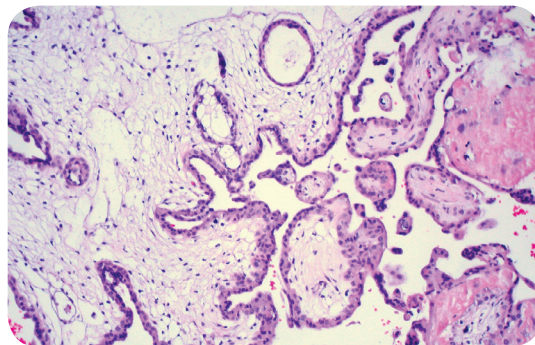


Figure 126.6 The histological appearance of a partial mole. In contrast to a complete mole, there will be both normal villi (right of image) and hydropic villi (left of image). Trophoblastic proliferation is minimal.